DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
5100 Paint Branch Parkway
College Park, Maryland 20740

APR 20 2004

Jim Prochnow
Greenberg Traurig, LLP
The Tabor Center
1200 17th Street, Suite 2400
Denver, Colorado 80202

Dear Mr. Prochnow:

This is to inform you that the notification, dated February 3, 2004, you submitted pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on February 6, 2004. Your notification identified the substance "Cotinine" (*Duboisa hopwoodii* (F. Muell.)) as the substance that you intend to market as a new dietary ingredient.

According to the notification, under conditions of use, you recommend "taking one (1) to four (4) tablets (or capsules) per day or as directed by health care provider. The amount per tablet or capsule will be adjusted to keep the daily serving within the range of 75 mg to 150 mg."

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under section 350b (a) (2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. 342(f) (1) (B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

Cotinine may be excluded from the definition of "dietary supplement" under 21 U.S.C. 321(ff)(3)(B). "Cotinine" is an article authorized for investigation as a drug for which substantial clinical investigations have been instituted in the United States, and the

investigations have been made public, and which was not before such authorization marketed as a dietary supplement or as a food. Because the information in your submission does not specify the form of your new dietary ingredient, we are unable to determine if your ingredient has been the subject of previous investigational new drug applications.

Your notification presents a novel issue for FDA to consider with respect to whether the product includes an article that has been approved as a new drug under 21 U.S.C. 355 (21 U.S.C.321(ff)(3)(B)(i)). Please provide a complete chemical description of your ingredient. FDA will then complete its evaluation shortly and send you a response to your notification explaining FDA's decision about whether your products are dietary supplements within the meaning of 21 U.S.C. 321(ff).

This letter is to alert you within the 75-day notification period that FDA has concerns about whether your product can lawfully be marketed as a dietary supplement. Please note that failure to respond to a notification within the 75-day timeframe does not constitute a finding by the agency that the ingredient or a product that contains the ingredient is safe or is not adulterated under 21 U.S.C. 342. 21 C.F.R.190.6(f).

If you have any questions concerning this matter, please contact Victoria Lutwak at (301) 436-2375.

Sincerely yours,

Susan J. Walker, M.D.
Director
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition